

of 37 C.F.R.121 (b)(i), applicants present the language of both the unchanged claims and the presently amended claims in clear copy format for pending claims 1-15 respectively.

Applicants' amendments are as follows:

In the Specification:

Page 7, line 24, after "Fig. 10 presents Table 4", insert - - [SEQ ID NO: 1] - -

In the Drawing

Please add new Fig. 10 as a complete substitution for the previously submitted Fig. 10

In the Claims:

Pending claims 1-15 respectively, as presently amended, are recited below in clear copy format.

1 (Twice Amended). A method for stimulating angiogenesis within a targeted collection of viable cells in-situ, said method comprising the steps of:

identifying a collection of cells comprising viable cells in-situ as a target for stimulation of angiogenesis;

providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;

introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using said effecting means;

allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby

- (a) the $\alpha 7$ subunit of at least some of the proteasomes interact with said PR-39 oligopeptide collective member, and
- (b) the proteolytic degradation of at least one identifiable peptide mediated by said proteasomes with an interacting $\alpha 7$ subunit becomes markedly inhibited while the proteolytic degradation mediated by said proteasomes with an interacting $\alpha 7$ subunit against other individual peptides remains unaltered, and
- (c) the markedly inhibited proteolytic degradation activity of said proteasomes with said interacting $\alpha 7$ subunit results in a stimulation of angiogenesis in-situ.

2 (Twice Amended). A method for altering proteasome-mediated degradation of peptides in-situ within a collection of viable cells, said method comprising the steps of:

- identifying a collection of cells comprising viable cells in-situ as a target;
- providing means for effecting an introduction of at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells;
- introducing at least one member of the PR-39 oligopeptide collective to the cytoplasm of said targeted collection of cells using effecting means;

allowing said introduced PR-39 oligopeptide collective member to interact with such proteasomes as are present within the cytoplasm of said targeted collection of cells whereby

- (a) the $\alpha 7$ subunit of at least some of the proteasomes interacts with the PR-39 oligopeptide collective member, and

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(b) the proteolytic degradation of at least one identifiable peptide mediated by said proteasomes with an interacting $\alpha 7$ subunit becomes markedly inhibited while the proteolytic degradation mediated by said interacting proteasomes with an interacting $\alpha 7$ subunit against other individual peptides remains unaltered, and

(c) the markedly inhibited proteolytic degradation of the proteasomes with said interacting $\alpha 7$ subunit results in an increased expression of said identifiable peptide in-situ within the targeted collection of cells.

3 (Original) The method as recited in claim 1 or 2 wherein said collection of viable cells includes at least one type of cell selected from the group consisting of endothelial cells, myocytes and myoblasts, fibrocytes and fibroblasts, epithelial cells, osteocytes and osteoblasts, neuronal cells and glial cells, erythrocytes, leukocytes, and progenitor cells of all types.

4 (Original) The method as recited in claim 1 or 2 wherein said collection of cells comprises at least one tissue selected from the group consisting of myocardium, skeletal muscle, smooth muscle, an artery, a vein, lung, brain, kidney, spleen, liver, gastrointestinal tissue, nerve tissue, limbs, and extremities.

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5 (Once Amended). The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member include one selected from the group consisting of catheter-based means, injection-based means, infusion-based means, localized

intravascular means, liposome-based means, receptor-specific peptide means, and slow releasing means for peptide secretion in living cells and sequestered organisms.

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nv

6 (Twice Amended). The method as recited in claim 1 or 2 wherein the means for an introduction of a PR-39 oligopeptide collective member includes DNA sequences coding for at least one PR-39 oligopeptide collective member in an expression vector for transfection and subsequent expression of the PR-39 oligopeptide collective member within said cells.

7 (Original) The method as recited in claim 1 or 2 wherein said method is practiced under in-vivo conditions.

8 (Original) The method as recited in claim 1 or 2 wherein said method is practiced under in-vitro conditions.

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9 (Once Amended). The method as recited in claim 1 or 2 wherein degradation of $\text{IK}\beta\alpha$ is inhibited.

C4

10 (Once Amended). The method as recited in claim 1 or 2 wherein degradation of HIF- 1 α is inhibited.

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3/20/01

11 (Twice Amended). A family of PR-39 derived oligopeptides whose members individually cause an inhibition of proteasome-mediated degradation of at least one

identifiable peptide in-situ after introduction intracellularly to a viable cell, each member of said PR-39 derived oligopeptide family

less than 26 amino acid residues in length;

an oligopeptide whose N-terminal amino acid residue sequence which begins with Arg-Arg-Arg;

at least partially homologous with the amino acid sequence of native PR-39 peptide;

pharmacologically active for markedly altering the proteolytic degradation activity of proteasomes in-situ;

able to interact in-situ with at least the $\alpha 7$ subunit of such proteasomes as are present within the cytoplasm of the cell; and

able to alter the proteolytic degradation activity of said proteasomes having an interacting $\alpha 7$ subunit such that the proteolytic degradation mediated by said proteasomes against at least one identifiable peptide becomes markedly inhibited while the proteolytic degradation mediated by said proteasomes against other individual peptides remains unaltered.

12 (Twice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 15 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-Arg-Pro-Pro [SEQ ID NO; 3].

Claim 13
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13 (Twice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 11 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg [SEQ ID NO: 4].

Claim 14
C8

14 (Twice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 8 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr [SEQ ID NO: 5].

Claim 15
C9

15 (Once Amended). A family of PR-39 derived oligopeptides whose members cause an inhibition of protease-mediated degradation of at least one identifiable peptide in-situ after introduction intracellularly to a viable cell, each member of said oligopeptide family being:

less than 20 amino acid residues in length;

an oligopeptide whose N-terminal amino acid residue sequence begins with ARG-
ARG-ARG;

at least partially homologous with the amino acid sequence of native PR-39 peptide;
pharmacologically active for markedly altering the proteolytic degradation activity
of proteasomes in-situ;

able to interact in-situ with at least the $\alpha 7$ subunit of such proteasomes as are present
within the cytoplasm of the cell; and

able to alter the proteolytic degradation activity of said proteasomes having an
interacting $\alpha 7$ subunit such that the proteolytic degradation mediated by said proteasomes
against at least one identifiable peptide becomes markedly inhibited while the proteolytic